REMARKS

Claims 9 and 10 have been amended. Claims 1-17 currently are pending.

To overcome 35 USC § 112, second paragraph rejections applicants amended claim 9 to delete "organisms" and substituted "the microorganisms." Also, claim 9 should recite "... and integrating said gene..." not "...integrating the said gene..." Claim 9 currently reads correctly.

The examiner rejected claim 3-17 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The examiner stated that applicants are claiming a genus of sequences encoding OMP-DC proteins with no correlation between the structure of the OMP-DC sequence and its function. The examiner stated that without a correlation between structure and function, the structure of other members of the genus which could be obtained by genetic engineering is unknown to applicants.

In response, applicants amend claim 10 so that now it is directed to an orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID NO: 1 or its homologs which have at least **90%** homology with SEQ ID NO: 1. These homologs are disclosed on page 3 (lines 26-44) and page 4 (lines 1-7) of the specification. The specification teaches on page 4 (lines 24-29) additional organisms such as members of the family Metschnikowiaceae such as the general Eremothecium, Ashbya, or Nematosproa from which the orotidine-5'-phosphate decarboxylase gene can be isolated. There is clear teaching in the specification about homologs and what is meant by the term "homologs."

The examiner believes that absent clear structure-function correlation the genus is not described because one would need to practice trial and error experimentation to make changes randomly in the gene sequence and screen for sequences that maintain biological activity.

Applicants disagree because deriving the homologs would be predictable. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. MPEP § 2163. Applicants believe one of ordinary skill in the art would recognize members of the genus (90% homologs) of the species disclose (SEQ ID NO: 1) because there are suitable methods which are readily available for determining whether a nucleic acid sequence has the recited degree of sequence homology and possess function.

Algorithms in computer program PileUp (J. Mol. Evolution, 25, 351-360, 1987, Higgins et al., CABIOS, 5 1989: 151-153) or the programs Gap and BestFit which are part of the GCG software package and which are disclosed by Needleman and Wunsch (J. Mol. Bio. 48: 443-453, 1970) and Smith and Waterman (Adv. Appl. Math. 2; 482-489, 1981) can be used to identify such homologs.

Also, one of ordinary skill in the art would know of many ura3 sequences from many sources such as from

http://www.biochem.ucl.ac.uk/bsm/pdbsum/1dv7/align_A.html or

http://www.stdgen.lanl.gov/cgi-

bin/gene_id_search.cgi?dbname=sage&gene_id=SAG1047. With this knowledge the skilled artisan easily can compare the sequences with standard programs. The different regions of a protein can be identified and modified by standard method which would retain the protein activity. Therefore, contrary to what the examiner stated one does not need to practice trial and error experimentation to make changes randomly in the gene sequence and screen for sequences that maintain biological activity.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such account.

Respectfully submitted,
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COMPLETE COPY OF ALL CLAIMS

1. (previously presented) An orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID NO: 1 which is isolated from microorganisms.

2. (previously presented) An orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID NO: 1 which is isolated from *Ashbya gossypii*.

3. (previously presented) An isolated amino-acid sequence encoded by a gene or its homologs as claimed in claim 1.

4. (previously presented) An isolated amino-acid sequence as claimed in claim 3, which comprises an enzymatically active protein.

5. (previously presented) A gene construct comprising an orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID No: 1 or its homologs as claimed in claim 1, where the gene or its homologs is functionally linked to one or more regulatory signals.

6. (original) A gene construct as claimed in claim 5, whose gene expression is increased by the regulatory signals.

7. (previously presented) A vector comprising a gene construct as claimed in claim 5.

8. (previously presented) A microorganism comprising at least one gene construct as claimed in claim 5.

9. (currently amended) A process for producing uracil-auxotrophic microorganisms, which comprises modifying an orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID NO: 1 or its homologs as claimed in claim 1 in such a way that the protein encoded by the gene is inactive, and introducing this modified gene into the

microorganisms and integrating said gene by homologous recombination into the genome of the microorganisms, and subsequently selecting these microorganisms for resistance to 5-fluoroorotic acid thereby producing uracil-auxotrophic microorganisms.

10. (currently amended) A process for inserting DNA into microorganisms, which comprises inserting a vector which comprises an intact orotidine-5'-phosphate decarboxylase gene having the sequence SEQ ID NO: 1 or its homologs isolated from microorganisms which have at least ~~80~~ 90% homology with the sequences SEQ ID NO: 1 as claimed in claim 1 together with at least one other nucleic acid sequence, into a microorganism which is deficient in orotidine-5'-phosphate decarboxylase nucleic acid sequence having the sequence SEQ ID NO: 1 and cultivating this microorganism on or in a culture medium without uracil.

11. (original) A process as claimed in claim 10, wherein a linear DNA is used as vector.

12. (previously presented) A process as claimed in claim 10, wherein an *Ashbya gossypii* strain is used as the microorganism deficient in orotidine-5'-phosphate decarboxylase genes.

13. (previously presented) A process as claimed in claim 10, wherein at least one gene of riboflavin synthesis is inserted as additional gene into the microorganism.

14. (previously presented) A process for selecting cells, said process comprising the step of transforming cells with a gene sequence or its homologs as claimed in claim 1 and selecting for the transformed cells.

15. (previously presented) The process as claimed in claim 14 wherein said cells are *Ashbya gossypii.*

16. (previously presented) Homologs having 80% homology with the orotidine-5'-phosphate decarboxylase gene claimed in claim 1.

17. (previously presented) Homologs of the orotidine-5'-phosphate decarboxylase gene claimed in claim 2.